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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/462,931	01/18/00	HELLMAN J	2328-115

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EXAMINER	
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ART UNIT	PAPER NUMBER
1641	10

DATE MAILED: 07/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/462,931	HELLMAN ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2001* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6, 8-13, and 18-24* is/are pending in the application.

4a) Of the above claim(s) *1-3, 12-13, and 18-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6 and 8-11* is/are rejected.

7)☒ Claim(s) *4-6 and 8-11* is/are objected to.

8)☒ Claims *1-6, 8-13, and 18-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Please note that the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Group Art Unit **1641**. All communications should be directed to **Lisa V. Cook**, whose telephone number is **(703) 305-0808**.

Election/Restrictions

2. Applicant's response/amendment (Paper#9) to the Restriction Requirement mailed 3/19/01 was carefully considered and found persuasive. Because the newly submitted amendments to the claims are specifically directed to an antibody binding Seq. Id. No.2, a cell line producing Seq. Id. No.2, and an assay to detect Seq. Id. No.2, the claims now have unity of invention properly belonging in one single group drawn to a single inventive concept. The following reformulated Restriction Requirement is presented to clarify the status/grouping of all the pending claims:

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains claims directed to more than one invention:

A. Group **I**, claim(s) 1-3 are drawn to an isolated osteocalcin fragment derived from human urine, classified in class 530, subclass 300 and class 530, subclass 350 for example. (A product – special technical feature).

B. Group **II**, claim(s) 4-6 and 8-11 are drawn to an antibody and its corresponding hybridoma cell, and an assay utilizing the antibody, classified in class 530, subclass 387.1 and class 436, subclass 326 for example. (A second product/second special technical feature and a process of making said product and process of utilizing the product).

C. Group **III**, claim(s) 14-17 are drawn to a non-competitive immunoassay to determine isolated osteocalcin fragments, classified in class 435, subclass 7.2 for example. (A process to detect isolated osteocalcin fragments – not limited to the special technical feature).

D. Group **IV**, claim(s) 12-13 and 18-24 are drawn to a methods of measuring the rate of bone turnover via isolated osteocalcin fragment detection, classified in class 436, subclass 512 for example. (A second process to detect isolated osteocalcin fragments – not limited to the special technical feature).

4. The following inventions or groups of inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1. In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention, to which the claims must be restricted.

5. The product of Group A - an isolated osteocalcin fragment constitutes the special technical feature. However, the other inventions are not related to processes specific for making and or using an isolated osteocalcin fragment. Therefore, Groups A , B, C, and D lack the same corresponding technical feature and do not relate to a single general inventive concept under PCT Rules 13.1 and 13.2.

6. The inventions listed as Groups A, B, C, and D do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The first sited technical feature is drawn to an isolated osteocalcin fragment (Group A) the other groups are not related to this special technical feature as specified under 37 CFR 1.475(b) so as to have unity of invention. An application or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.

(d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and **do not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes foreign patents and applications as well as literature searches.

8. Applicant's election without traverse of reformulated Group II (claims 4-6 and 8-11) in Paper No. 9 is acknowledged.

The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

9. Claims 7 and 14-17 were inclusively cancelled be applicant. Currently claims 1-3, 12-13, and 18-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No.9. Claims 4-6 and 8-11 are pending and currently under consideration.

Priority

10. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does not contain the required first sentence of the specification referencing 371 document PCT/FI98/00550 filed 6/24/98 and foreign application No. 973371 filed 8/15/97 in Finland. Please add to the specification.

Drawings

11. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the examiner allows the application.

Information Disclosure Statement

12. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

Specification

13. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claim 4 is directed to non-statutory subject matter. The invention as claimed reads on any monoclonal antibody, where antibody as a genus includes naturally occurring as well as synthetic compositions. Nonnaturally occurring compositions are considered to be patentable subject matter with in the scope of 35 U.S.C. 101, but products occurring in nature are considered non-statutory and non-patentable. See Official Gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated" or "purified" to overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 4-6 and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 4 and 6 are vague and indefinite because it is not clear what the monoclonal antibody will bind. As recited the monoclonal antibody is directed to any composition comprising the entire seq. Id. no.2 (lines 1-8 in the claims), monoclonal antibodies which bind fragments from amino acid position 7 to position 30 of seq. Id. no.2, and monoclonal antibodies which bind fragments from amino acid position 6 to position 30 of seq. Id. no.2. It is not clear if applicant intends the monoclonals of the instant invention to binding the full sequence of seg. Id. no.2 or fragments thereof? Please clarify.

B. Claims 9-11 are vague and indefinite in the use of the acronyms 2H9, 6F9, 1C4, and 3H8. The terms should be defined in their first instance or referred to their intended structural definitions. It is not clear if applicant intends for the acronyms to be defined by the prior art teachings. The prior art may utilize the same laboratory designations therein reading on the instant claims, it is suggested that monoclonals of this type include Atcc deposit/accession

numbers or seq. Id. nos. for proper identification. Please identify applicants intended meaning/define.

C. Claims 6-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are explained below:

The claims particularly, independent claim 6 is drawn to an assay method that employs antibodies. The antibodies bind with sequence identification no. 2, but the method does not indicate that a complex will be formed or identified (i.e.label). The method does not outline how bound complex will be separated from unbound complexes or how the complex will be correlated to seq. Id. no. 2 via detection. The recitation of a method as recited in claim 6 requires at least a contact step, a separation step, a detection step, and a correlation step. Please include the appropriate steps.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 4-6 and 8-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth monoclonal antibodies 2H9, 6F9, 3G8, 1C4, and 3H8 and therefore the written description is not

commensurate in scope with the claims drawn to any monoclonal antibody that binds Seq. Id. No.2 (recited in independent claims 4 and 6). See pages 16-22.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is several from its enablement provision (see page 115).

With the exception of Mab's 2H9, 6F9, 3G8, 1C4, and 3H8, the skilled artisan cannot envision the detailed structure of the encompassed monoclonal antibodies and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The monoclonal antibody itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of

a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus.

At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention" There is insufficient description in the disclosure to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore only the isolated Mab's 2H9, 6F9, 3G8, 1C4, and 3H8, but not any monoclonal that competes with the monoclonal antibodies would meet the full breadth of the claims as required by the written description provision of 35 USC 112, first paragraph.

17. Claims 4-6 and 8-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of monoclonal antibodies 2H9, 6F9, 3G8, 1C4, and 3H8. Because it is not clear that the properties of monoclonal antibodies 2H9, 6F9, 3G8, 1C4, and 3H8 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the monoclonal antibodies 2H9, 6F9, 3G8, 1C4, and 3H8, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production monoclonal antibodies, one of ordinary skill in the art could be

assured to the ability to practice the invention as claimed. Exact replication of the monoclonal antibodies is an unpredictable event.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record that has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1)The name and address of the depository;

2)The name and address of the depositor;

3)The date of deposit;

4)The identity of the deposit and the accession number given by the depository;

5)The date of the viability test;

6)The procedures used to obtain a sample if the test is not done by the depository; and

7)A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

18. For reasons aforementioned, no claims are allowed.

Remarks

19. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Hellman et al. (Journal of Bone Mineral Research, Vol.11., No.8., 1996, pages 1165-1175) disclose nine monoclonal antibodies against osteocalcin via two-site assay procedures.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
(703) 305-0808
06/25/01

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641